REMARKS

In view of the foregoing amendments and the following representations, reconsideration and allowance of the above-identified application is respectfully requested.

Claims 1-31 are in the present action. In the present response, Applicants have amended the claims to clearly indicate that the claimed dosage forms consist of (a) a controlled release core containing a biguanide drug as the only active ingredient in the core; (b) a seal coat applied to the controlled release core; and (c) an immediate release coating that is applied to the seal coating. The immediate release coating contains a thiazolidinedione derivative that is released from the dosage from in an immediate manner.

Claims 11-31 as originally filed did not require the presence of a seal coating between the controlled release core and the immediate release coating. Applicants will pursue claims directed to a dosage form without the seal coat between the controlled release core and immediate release layer in a subsequent application.

On page two of the Office Action, the Examiner provisionally rejected claims 1, 2, 4-6, 8-10 and 20-35 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 20 and 33-40 of copending Application No. 11/094,493. In response to this provisional rejection, the Applicants agree to submit a terminal disclaimer in this and/or the copending application if allowed claims are obtained in this and the copending application and the Examiner maintains the nonstatutory obviousness-type double patenting rejection.

On page 3 of the Office Action the Examiner rejected claims 1-10 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. Specifically, the Examiner indicated a confusion regarding the seal coat requirement in claims 1-20. In response to this rejection, Applicants have amended the pending claims to specifically indicate that the claimed dosage forms require the presence of a seal coat between the controlled release biguanide core and the immediate thiazolidinedione coating. See independent claims 1, 11, 21 and 31. All the claims as originally filed did not require the seal coat between the controlled release biguanide core and the immediate release thiazolidinedione coating. As currently amended the only "optional" seal coat language appears in dependent claims 3, 13, 23 and independent claim 31. These claims have been amended to indicate that the "optional" seal coat is a seal coat between the osmotic core and semipermeable membrane of the osmotic tablet. More specifically, claims 3, 13, 23 and 31 require that the "controlled release biguanide core" be an osmotic tablet comprising: (i) a biguanide core; (ii) an optional seal coat applied to the biguanide osmotic core; and (iii) a semipermeable membrane surrounding the core and optional seal coat to create the osmotic tablet. It is respectfully submitted that the amendments to claims 11, 21 and 31 requiring the presence of a seal coat between the controlled release biguanide core and the plain language of claims 3, 13, 23 and 31 overcomes the Examiner's rejection of claims 1-10 under 35 U.S.C. § 112, second paragraph.

On pages 3 and 4 of the Office Action the Examiner rejected claims 1-5, 7-15, 17-25 and 27-30 under 35 U.S.C. § 112, second paragraph because the term "thiazolidinedione

derivative" is indefinite. Applicants respectfully traverse this rejection. Page 1, lines 11-12 of the specification states that the thiazolidinedione derivatives are described in U.S. Patent No. 4,687,777. A similar statement is contained on p. 2, line 14 of the specification. Page 5, line 33-34 of the specification states: "The term thiazolidinedione derivative as used in this specification refers to drugs that are useful for controlling or managing NIDDM". It is respectfully submitted that these portions of the specification clearly define the term "thiazolidinedione derivative" to an individual of ordinary skill in the art as a compound having the basic structure disclosed in U.S. Patent No. 4,687,777 and that is useful for controlling or managing NIDDM. Applicants respectfully request reconsideration of this rejection.

On page 4 of the Office Action, the Examiner rejected claims 7, 17 and 27 under 35 U.S.C. § 112, second paragraph because the term "substantially free" is indefinite and not supported by the specification. In response to this rejection, Applicants have amended claims 7, 17 and 27 to delete the "substantially free" terminology and replaced it with the language that appears on page 3, lines 17-20 of the specification. No new matter is added by this amendment and it is respectfully submitted that this amendment overcomes the rejection of claims 7, 17 and 27 under 35 U.S.C. § 112, second paragraph.

On pages 4-8 of the Office Action the Examiner rejected claims 1-31 under 35 U.S.C. § 103(a) as being unpatentable over the teachings of Vergez et al., United States Published Patent Application No. 2006/0204578 ("Vergez").

In response to this rejection Applicants have amended the claims to specifically indicate that the claimed dosage form requires three separate and distinct elements.

Specifically each claim now requires 1) a controlled release biguanide core; 2) a seal coat applied to the biguanide controlled release core; and 3) an immediate release thiazolidinedione derivative coating. The controlled release core can be any type of controlled release core such as a hydrogel matrix or osmotic tablet but it can contain only one pharmaceutically active ingredient, a biguanide, and specifically metformin as recited in claims 4, 14, 24 and 31.

The amendments reciting the controlled release core "consists essentially of" a biguanide and at least one pharmaceutically acceptable excipient is intended to limit the controlled release core to a single pharmaceutically active component and not to a specific type of controlled release core or release controlling excipient. This fact is evident from the dependent claims that further define the controlled release core such as claims 3 and 7. No new matter is added by these amendments. Support can be found in claims 1 and 4 as originally filed.

Applicants have also amended claims 4, 14 and 24 to recite that the biguanide in the controlled release core is metformin hydrochloride and the thiazolidinedione derivative is pioglitazone hydrochloride. No new matter is added by these amendments. Support can be found in Examples 1-6 of the specification.

During the course of development of the claimed dosage form, Applicants encounter a number of problems associated with combining two completely different drugs such as metformin and pioglitazone. For example, metformin hydrochloride, a biguanide, is a freely soluble drug while pioglitazone hydrochloride, a thiazolidinedione derivative, is a practically insoluble drug. Faced with these vastly different solubility

issues, the Applicants need to design a dosage form that would delay the dissolution of the water soluble metformin while promoting the dissolution of the insoluble pioglitazone. To resolve these issues, Applicants elected to isolate the metformin in a controlled release core and place the pioglitazone in an immediate release coating around the controlled release core.

After conducting numerous experiments, Applicants encountered further problems with the immediate thiazolidinedione derivative layer. For example, it was found that the immediate release layer would not adhere to the controlled release core or it would adhere to well and not release the thiazolidione derivative in a timely manner. It was also discovered that the composition of the immediate release coating affected the stability of the thiazolidinedione derivative.

In order to overcome some of these problems, Applicants discovered that a seal coat between the immediate release thiazolidinedione derivative layer and the biguanide controlled release core resulted in a dosage form that provided good adhesion for the immediate release thiazolidinedione layer to the dosage form, allowed for the release of the thiazolidinedione derivative in a timely manner and produced a stable product.

The Vergez reference does not disclose or remotely suggest the invention recited in the pending claims. The Vergez reference teaches a controlled release dosage form where two different drugs are released from the dosage form in a controlled manner. See ¶ 15. The pending claims require that only the biguanide component be released in a controlled manner and the thiazolidinedione derivative be released immediately (not controlled). The Vergez reference does indicate that an immediate release layer could be added to the

dual drug controlled release core but it does not provided any guidance on the manner in which the immediate release coat could be applied or its composition. The Vergez reference merely provides a broad general teaching on how to provide an additional drug layer to the dual drug controlled release core. See ¶ 63.

The Examiner is correct that the Vergez reference does suggest that a combination of two antidiabetic drugs could be used in the controlled release core but it does not suggest the specific combination of a controlled release biguanide and an immediate release thiazolidinedione as recited in the pending claims.

The working examples of the Vergez reference also fails to provide any guidance in arriving a the present invention. First, none of these examples employ an immediate release drug layer. Second, none of the examples describe a dosage form with only a single drug in the controlled release core. Third, none of the examples provide guidance for preparing a biguanide controlled release core or any type of biguanide dosage form. Example 7 in ¶ 190 of the Vergez reference does employ a thiazolidinedione derivative, pioglitazone, but this example is designed to release the pioglitazone in a controlled or sustained manner, not an immediate release manner as recited in the pending claims. Example 7 also employs atorvastatin calcium which is a very slightly soluble drug (See ¶ 156 of the Vergez reference) which is quite different from the freely soluble biguainde, metformin recited in the pending claims.

Because the pending claims require a controlled release core with a single active ingredient and an immediate release thiazolidinedione layer with a seal coating between the controlled release core and the thiazolidinedione layer, a combination that is not

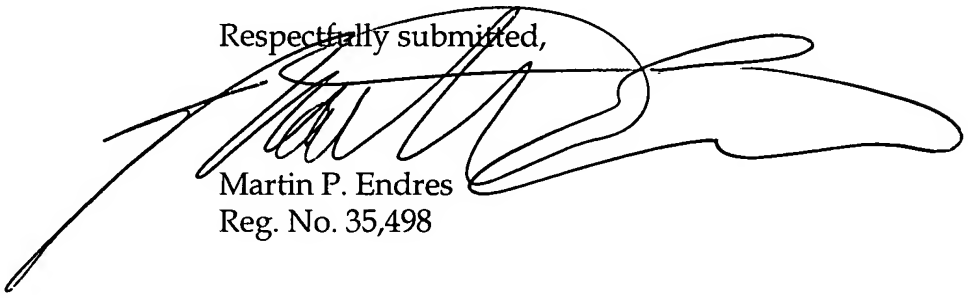
suggested or disclosed in the Vergez reference, it is respectfully submitted that the pending claims are patentable over the Vergez reference. Applicants also respectfully submit that claims 4, 14 and 24 are patentable over the Vergez reference because these claims specifically recite the combination of the freely soluble metformin HCl and the insoluble pioglitazone HCl . This combination in the manner recited in the pending claims is not disclosed or suggested by the Vergez reference.

It is respectfully submitted that it would NOT be a mere matter of design choice to prepare a biguanide controlled release core, apply a seal coating to the controlled release core and then apply an immediate release thiazolidinedione derivative coating to the seal coat in light of the teachings of the Vergez reference. This contention is improperly using hindsight especially in light of the numerous issues discussed above which the Applicants encountered during development of the dosage form. Based upon the broad disclosure of the Vergez reference there is no expectation of success nor any guidance on how to arrive at the presently claims invention.

Based upon the foregoing amendments and representations, Applicants respectfully submit that the rejection of the claims in the above-identified application have been overcome and should be withdrawn. Early and favorable action is earnestly solicited.

It is believed that no fee is required for submission of this response because it is being mailed before the three month deadline, February 15, 2007. If a fee is due, the Commissioner is authorized to charge our deposit account, Account No. 08-1540.

Respectfully submitted,



Martin P. Endres
Reg. No. 35,498

MAILING ADDRESS:
HEDMAN & COSTIGAN, P.C.
1185 Avenue of the Americas
New York, NY 10036-2601
(212) 302-8989